REMARKS

Claims 39-41, 43-45, 48-56, and 59-62 are pending. No new matter has been added by way of the present amendments. For instance, claim 39 has been amended to define a method for simultaneously exposing an array of test compounds to a detector layer of physiologically viable cells. In particular, as supported by originally filed claims 15 and 16, claim 39 has been amended to specify the procedure wherein an array of test compounds is brought into contact with a detector layer comprised of physiologically viable cells. This amendment highlights an important feature of the invention: the ability to control lateral diffusion of the test-substances. As specified in detail e.g., on page 13, the porous membrane will, due to orthogonal capillarity, limit lateral spread of test compounds applied to the membranes. The dependency of other claims has also been amended. New claim 60 is supported by the present specification at page 4, last full paragraph. New claim 60 is similar to claim 39, but adds the step of detecting the response in the detector layer. Lastly, new claims 61 and 62 are supported by the present specification at page 13. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Formal Drawings

At page 2 of the office action dated April 26, 2001, the Examiner indicated that the drawings were informal. However, Applicants have not yet received a Notice of Draftsperson Review concerning the present drawings. Accordingly, Applicants request that the USPTO issue a Notice of Draftsperson Review indicating what aspects of the drawings are considered informal.

Issues under 35 USC § 112, second paragraph

The Examiner has rejected claims 39-58 for the reasons recited at pages 3-4 of the outstanding office action. Applicants respectfully traverse each of these rejections.

First, the Examiner asserts that claim 39 is indefinite for the recitation of steps b), c) and d) as well as for allegedly omitting an essential step. Applicants submit that claim 39 has been substantially amended and each of the Examiner's rejections are moot. Reconsideration and withdrawal thereof are requested.

Second, the Examiner asserts that claim 58 is ambiguous. Applicants submit that claim 58 has been cancelled, thus, this

rejection is moot. Reconsideration and withdrawal thereof are requested.

In view of the above, Applicants submit that the presently pending claims fully satisfy the requirements of 35 USC § 112, second paragraph. Thus, the Examiner is requested to withdraw these rejections.

Issues under 35 USC § 102(e)

The Examiner has rejected claims 39, 41-45, 51, 53, 54, 56, 58 and 59 as being anticipated by Negulescu et al., USP 6,214,563 (hereinafter referred to as Negulescu '563). Applicants respectfully traverse this rejection.

Negulescu '563 relates to a method for screening test chemicals in fluorescent assays using photon reducing agents. The method of Negulescu '563 involves a well-based array which requires sophisticated technologies to dispense micro-volumes of many different fluids to selected locations. Negulescu '563 fails to disclose bringing the support holding the compounds in close apposition with the detector layer as presently claimed. Nor does Negulescu '563 disclose passing the compounds through a porous membrane or the use of diffusion to allow the compounds to pass through the membrane. Accordingly, Negulescu '563 fails to anticipate the present claims.

Applicants further point out that claim 39 requires "simultaneously exposing an array of test compounds to a detector layer of physiologically viable cells." Since Negulescu '563 discloses separate testing of each compound, such "simultaneous exposure" as claimed is impossible. Thus, claim 39 is further distinguished from Negulescu '563.

The Examiner has rejected claims 39-42, 45, 48, 49, 51-55, 58 and 59 as being anticipated by Chelsky et al., USP 5,856,083 (hereinafter referred to as Chelsky '083). Applicants respectfully traverse this rejection.

Chelsky '083 relates to an assay for compounds that affect enzyme activity or bind to target molecules. However, Chelsky '083 fails to suggest or disclose the use of either a porous membrane or the use of physiologically viable cells as the detector layer. Accordingly, the present claims, which require these features, are not anticipated by Chelsky '083. Therefore, the Examiner is requested to withdraw the anticipation rejection based upon Chelsky '083.

Issues under 35 USC § 103(a)

The Examiner has rejected claims 46, 47, 50 and 57 as being anticipated by Chelsky '083 in view of Sittampalam et al.,

Current Opinion in Chemical Biology (hereinafter referred to as Sittampalam). Applicants respectfully traverse this rejection.

Distinctions Between the Present Invention and the Cited Art

As discussed above, Chelsky '083 fails to disclose the use of a porous membrane or physiologically viable cells. The Examiner asserts that based upon the disclosure of Sittampalam, one of skill in the art would use the physiologically viable cells of Sittampalam on the solid matrix of Chelsky '083. Applicants respectfully disagree with the Examiner. In fact, one having ordinary skill in the art would not make such a modification of Chelsky '083.

Providing test compounds in a non-well format solves the problem of liquid handling. However, diffusion between compound "zones" is the problem facing the screening person. Chelsky '083 solves the problem by using a colloidal matrix (refer to Column 5, lines 43-53 of Chelsky '083. The present invention addresses the problem differently, and does so for good reasons.

First, the present claims involve the use of live cells in the assay as the detector layer. When physiologically viable cells constitute the detector layer, they should be maintained under physiologically viable conditions. Providing such physiologically viable conditions requires the use of solutions

able to supply essential nutrients and able to buffer pH changes normal to the continued growth of physiologically viable cells. Physiologically viable cells also require gases essential to continued cell growth and maintenance of buffer capacity (O_2, and optionally 5% CO_2, depending on the type of buffer being used) (see page 14, last paragraph of the present specification). Accordingly, physiologically viable cells cannot sit in a colloidal matrix (as required by Chelsky '083). Therefore, the Examiner's proposed modification of Chelsky '083 is improper.

Second, even if Chelsky '083 attempted the assay in a non-gelled aqueous environment, diffusion, convection, and agitation would mix the entire detection layer together, and thus make it impossible to spatially resolve the different sub-regions of the layer. For this additional reason, the Examiner's proposed rejection is improper.

One technological contribution to the art described in the present claims involves controlling the lateral diffusion of test compounds added to a layer of physiologically viable cells. The present invention allows vertical diffusion of the compounds through a porous membrane but, as specified in detail e.g., on page 13 of the present specification, due to orthogonal capillarity, the porous membrane will limit lateral spread of test compounds applied to the membrane. This aspect of the

invention is specifically defined in claims 39, 48, 60, 61 and 62. However, this aspect of the present claims is neither suggested nor disclosed by either of Chelsky '083 or Sittampalam. Thus, the Examiner's rejection is improper. Reconsideration and withdrawal thereof are requested.

In summary, the Examiner has failed to present either a valid case of anticipation or a valid *prima facie* case of obviousness. Thus, the Examiner is requested to withdraw all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie (Reg. No. 42,874) at the (703) 205-8000 to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of one (1) month to March 5, 2003 in which to file a reply to the Office Action. The required fee of $55.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any

additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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LRS/CAM

Version with Markings to Show Changes Made

IN THE CLAIMS:

Claims 42, 46, 47, 57 and 58 were cancelled.

The claims were amended as follows:

39. (Twice Amended) A method for simultaneously exposing an array of test compounds to a detector layer of physiologically viable cells [screening test compounds for bioactivity], comprising:

(a) providing an array of test compounds, wherein each test compound is disposed on a [solid] support [in a pattern whereby the identity of each said test compounds is indicated by a 2-dimensional coordinate]; and

(b) bringing the array of test compounds in close apposition with [a] the detector layer so that a porous membrane is in contact with a liquid layer surrounding the detector layer and is in contact with the array of test compounds thereby allowing diffusion of the test compounds through the porous membrane to the detector layer [,

(c) detecting a response of the detector layer to the test compound, wherein a response is indicative that a test compound is a bioactive compounds, and

(d) determining the identity of said bioactive compound by reference to the 2-dimensional coordinate of said bioactive compound].

40. (Amended) The method of claim 39, wherein the [solid] support is the [a] porous membrane.

41. (Amended) The method of claim 39, wherein the [solid] support is a non-porous substrate.

43. (Amended) The method of claim 39 [42], wherein the physiologically viable cells form a monolayer.

44. (Amended) The method of claim 39 [42], wherein the physiologically viable cells are supported by an optically clear substrate.

45. (Amended) The method of claim 60 [claims 39, 40 or 41], wherein the response is recorded by a sequence of images.

50. (Amended) The method of claim 41, wherein the solid support is a non-porous substrate and wherein the cells are grown on [a] the porous membrane, whereby the test compounds are allowed to diffuse though the porous membrane to the cells layer.

53. (Amended) The method of claim 60 [42], wherein the detected response is a change in a luminescence property of the physiologically viable cells in the detector layer.

54. (Amended) The method of claim 60 [42], wherein the detected response is a change in a fluorescence property of the physiologically viable cells in the detector layer.

55. (Amended) The method of claim 40, wherein the array of test compounds is generated on the [solid] support by combinatorial chemistry.

59. (Amended) A method for screening test compounds for bioactivity, comprising:

(a) contacting an array of test compounds with a detector layer whereby each test compound comes into contact with a localized liquid which is in contact with the

detector layer, wherein said array of test compounds is comprised of a plurality of test compounds, each of said test compounds being disposed on a solid support, and wherein said detector layer is comprised of a monolayer of physiologically viable cells; and

(b) detecting a response of the detector layer to the test compound, wherein a response is indicative that a test compound is a bioactive compound.

Claims 60-62 were added.